

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	"6355237" and repair	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:01
L2	9	"6355237"	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:01
L3	6	l2 and tissue	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:02
L4	4	l3 and angiogenesis	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:14
L5	290	leptin and growth adj promot\$4	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:14
L6	1	l5 and @py<"2000"	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:15
L7	28	l5 and @py<"2003"	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:17
L8	2	l5 and tissue adj maint\$5	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:18
L9	26	leptin and tissue adj maint\$5	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:19
L10	30	vasculogen\$5 and tissue adj maint\$5	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:24
L11	0	rocio near sierra-honigmann	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:24
L12	0	rocio near sierra	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:24
L13	1	rocio near S	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:25
L14	0	rocio near honigmann	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:25
L15	38	sierra near honigmann	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:26

## EAST Search History

L16	0	sierra near honigmann near rocio	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:25
L17	1	sierra near honigmann near R	US-PGPUB; USPAT; DERWENT	OR	ON	2006/10/11 12:25

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(FILE 'HOME' ENTERED AT 12:28:50 ON 11 OCT 2006)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 12:29:08 ON 11 OCT 2006

E ROCIO SIERRA-HONIGMANN /AU

L1 1 S E2  
L2 36957 S LEPTIN  
L3 107140 S ANGIOGEN?  
L4 308456 S REPAIR  
L5 17 S L2 (L) L3 (L) L4  
L6 8 DUP REM L5 (9 DUPLICATES REMOVED)

L6 ANSWER 1 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI The choroid plexus-cerebrospinal fluid system: From development to aging.  
 AU Redzic, Zoran B. [Reprint Author]; Preston, Jane E.; Duncan, John A.;  
 Chodobski, Adam; Szmydynger-Chodobska, Joanna  
 PY 2005  
 SO Schatten, GP [Editor]. Curr. Top. Dev. Biol., (2005) pp. 1-52. Current  
 Topics in Developmental Biology.  
 Publisher: ELSEVIER ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN  
 DIEGO, CA 92101-4495 USA. Series: CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY.  
 CODEN: CTDBA5. ISSN: 0070-2153. ISBN: 0-12-153171-6(H).  
 AB. . . More recent studies suggest, however, that the CP-CSF system plays a  
 much more active role in the development, homeostasis, and repair  
 of the central nervous system (CNS). The highly specialized choroidal  
 tissue synthesizes trophic and angiogenic factors,  
 chemorepellents, and carrier proteins, and is strategically positioned  
 within the ventricular cavities to supply the CNS with these biologically.  
 . . . the blood-CSF barrier (BCSFB), controls the entry of nutrients, such  
 as amino acids and nucleosides, and peptide hormones, such as  
 leptin and prolactin, from the periphery into the brain. The CP  
 also plays an important role in the clearance of toxins. . . . of  
 neuronal differentiation in various brain regions. In the adult CNS, the  
 CP appears to be critically involved in neuronal repair  
 processes and the restoration of the brain microenvironment after  
 traumatic and ischemic brain injury. Furthermore, recent studies suggest  
 that the. . .

L6 ANSWER 2 OF 8 MEDLINE on STN DUPLICATE 1  
 TI Impaired revascularization in a mouse model of type 2 diabetes is  
 associated with dysregulation of a complex angiogenic-regulatory network.  
 AU Schiekofer Stephan; Galasso Gennaro; Sato Kaori; Kraus Benjamin J; Walsh  
 Kenneth  
 PY 2005  
 SO Arteriosclerosis, thrombosis, and vascular biology, (2005 Aug) Vol. 25,  
 No. 8, pp. 1603-9. Electronic Publication: 2005-05-26.  
 Journal code: 9505803. E-ISSN: 1524-4636.  
 AB OBJECTIVE: Diabetes is a risk factor for the development of cardiovascular  
 diseases associated with impaired angiogenesis or increased  
 endothelial cell apoptosis. METHODS AND RESULTS: Here it is shown that  
 angiogenic repair of ischemic hindlimbs was impaired in  
 Lepr(db/db) mice, a leptin receptor-deficient model of diabetes,  
 compared with wild-type (WT) C57BL/6 mice, as evaluated by laser Doppler  
 flow and capillary density analyses. . . . and WT mice before and after  
 hindlimb ischemia using Affymetrix GeneChip Mouse Expression Set  
 microarrays. The expression patterns of numerous angiogenesis  
 -related proteins were altered in Lepr(db/db) versus WT mice after  
 ischemic injury. These transcripts included neuropilin-1, vascular  
 endothelial growth factor-A, placental. . . . CONCLUSIONS: These data  
 illustrate that impaired ischemia-induced neovascularization in type 2  
 diabetes is associated with the dysregulation of a complex  
 angiogenesis-regulatory network.

L6 ANSWER 3 OF 8 MEDLINE on STN  
 TI The choroid plexus-cerebrospinal fluid system: from development to aging.  
 AU Redzic Zoran B; Preston Jane E; Duncan John A; Chodobski Adam;  
 Szmydynger-Chodobska Joanna  
 PY 2005  
 SO Current topics in developmental biology, (2005) Vol. 71, pp. 1-52.  
 Journal code: 0163114. ISSN: 0070-2153.  
 AB. . . More recent studies suggest, however, that the CP-CSF system  
 plays a much more active role in the development, homeostasis, and  
 repair of the central nervous system (CNS). The highly  
 specialized choroidal tissue synthesizes trophic and angiogenic  
 factors, chemorepellents, and carrier proteins, and is strategically

positioned within the ventricular cavities to supply the CNS with these biologically. . . the blood-CSF barrier (BCSFB), controls the entry of nutrients, such as amino acids and nucleosides, and peptide hormones, such as leptin and prolactin, from the periphery into the brain. The CP also plays an important role in the clearance of toxins. . . of neuronal differentiation in various brain regions. In the adult CNS, the CP appears to be critically involved in neuronal repair processes and the restoration of the brain microenvironment after traumatic and ischemic brain injury. Furthermore, recent studies suggest that the. . .

L6 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 2  
 TI Common gene polymorphisms and nutrition: emerging links with pathogenesis of multifactorial chronic diseases (review).  
 AU Loktionov Alexandre  
 PY 2003  
 SO The Journal of nutritional biochemistry, (2003 Aug) Vol. 14, No. 8, pp. 426-51. Ref: 298  
 Journal code: 9010081. ISSN: 0955-2863.  
 AB . . . be affected by polymorphisms in the genes encoding taste receptors and a number of peripheral signaling peptides such as insulin, leptin, ghrelin, cholecystokinin, and corresponding receptors. Polymorphic central regulators of energy intake include hypothalamic neuropeptide Y, agouti-related protein, melanocortin pathway factors, . . . metabolism and their interactions with diet. Cancer-associated polymorphisms are discussed for groups of genes encoding enzymes of xenobiotic metabolism, DNA repair enzymes, factors involved in the cell cycle control, hormonal regulation-associated proteins, enzymes related to DNA methylation through folate metabolism, and angiogenesis-related factors. There is an apparent progress in the field with hundreds of new gene polymorphisms discovered and characterized, however firm evidence. . . energy homeostasis is a fundamental problem insufficiently investigated in this context so far. Impacts of genetic variation on systems controlling angiogenesis, inflammatory reactions, and cell growth and differentiation (comprising regulation of the cell cycle, DNA repair, and DNA methylation) are also largely unknown and need thorough analysis. These goals can be achieved by complex simultaneous analysis. . .

L6 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 3  
 TI Appearance of leptin in wound fluid as a response to injury.  
 AU Marikovsky Moshe; Rosenblum Charles I; Faltin Zehava; Friedman-Einat Miriam  
 PY 2002  
 SO Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society, (2002 Sep-Oct) Vol. 10, No. 5, pp. 302-7.  
 Journal code: 9310939. ISSN: 1067-1927.  
 AB The adiposity hormone leptin regulates food intake, body weight, reproduction and other metabolic and endocrine functions mainly through signaling to the hypothalamus. Leptin signaling to peripheral tissues other than the hypothalamus has been suggested for a number of processes such as immunity, bone metabolism, hematopoiesis, angiogenesis, and wound healing. It was previously shown that exogenously applied leptin accelerated wound healing and that leptin mRNA is expressed at the wound site, but there is no published evidence showing that it is translated into leptin protein that is available at the site of repair. To address this question we analyzed pig wound fluids collected from partial-thickness excisional wounds during the first 9 days after injury. Leptin was measured using a modified culture of HEK-293 cells, expressing both the human leptin receptor gene and the firefly luciferase gene driven by a STAT-inducible promoter. Relatively high levels of leptin activity (50-250 ng/ml) were detected in wound

fluids using the leptin receptor expressing HEK-293 cells. Our results suggest that leptin is normally induced (4.8- to 10.2-fold) in wound tissue during the first few days following injury and may operate in a paracrine or autocrine circuit during the wound repair process.

- L6 ANSWER 6 OF 8 MEDLINE on STN DUPLICATE 4  
TI Systemically and topically supplemented leptin fails to reconstitute a normal angiogenic response during skin repair in diabetic ob/ob mice.  
AU Stallmeyer B; Pfeilschifter J; Frank S  
PY 2001  
SO Diabetologia, (2001 Apr) Vol. 44, No. 4, pp. 471-9.  
Journal code: 0006777. ISSN: 0012-186X.  
TI Systemically and topically supplemented leptin fails to reconstitute a normal angiogenic response during skin repair in diabetic ob/ob mice.  
AB . . . AIMS/HYPOTHESIS: In diabetic patients impaired wound healing conditions are a therapeutic problem of clinical importance. Recently, we showed that supplemented leptin induced an acceleration of impaired wound closure in diabetic ob/ob mice by reversion of the delayed re-epithelialization process. Additionally, angiogenesis is central to a normal repair. As leptin has been reported to represent an angiogenic factor, we hypothesized that leptin-mediated angiogenic processes at the wound site might participate in leptin-mediated improvement of disturbed repair in ob/ob mice. METHODS: Using a model of excisional wounding, C57BL/6J-ob/ob mice were treated systemically and topically with recombinant murine leptin during the phase of repair. Changes in blood glucose concentrations and body weight were monitored. We measured expression of the vascular endothelial growth factor (VEGF) and the endothelial cell marker protein CD31 as a read-out for angiogenic processes at the wound site. RESULTS: Expression of VEGF protein upon injury was reduced (30 to 40%) in ob/ob mice compared with wild-type C57BL/6 animals. Systemic and topical administration of leptin reconstituted normal wound VEGF expressions but failed to reverse the strongly reduced angiogenic response in ob/ob mice. Immunohistochemistry confirmed that the epithelium and blood vessels located in the granulation tissue expressed the functional leptin receptor obRb isoform during skin repair. CONCLUSION/INTERPRETATION: These data suggest that leptin reconstituted epithelial expression of VEGF during skin repair in ob/ob mice but failed to improve wound angiogenesis in the granulation tissue. Thus, the accelerated wound closure observed in leptin-supplemented ob/ob mice is not coupled to an improved wound angiogenesis.
- L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
TI Leptin and wound healing: Systemically and topically supplemented leptin fails to reconstitute a normal angiogenic response during skin repair in diabetic ob/ob mice.  
AU Wetzler, Christian [Reprint author]; Stallmeyer, Birgit [Reprint author]; Pfeilschifter, Josef [Reprint author]; Frank, Stefan [Reprint author]  
PY 2001  
SO Naunyn-Schmiedeberg's Archives of Pharmacology, (2001) Vol. 363, No. 4 Supplement, pp. R79. print.  
Meeting Info.: 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology. Mainz, Germany. March 13-15, 2001. German Society for Experimental and Clinical Pharmacology and Toxicology.  
CODEN: NSAPCC. ISSN: 0028-1298.  
TI Leptin and wound healing: Systemically and topically supplemented leptin fails to reconstitute a normal

angiogenic response during skin repair in diabetic ob/ob mice.

L6 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 5  
TI Systemically and topically administered leptin both accelerate wound healing in diabetic ob/ob mice.  
AU Ring B D; Scully S; Davis C R; Baker M B; Cullen M J; Pelleymounter M A; Danilenko D M  
PY 2000  
SO Endocrinology, (2000 Jan) Vol. 141, No. 1, pp. 446-9.  
Journal code: 0375040. ISSN: 0013-7227.  
AB Leptin is a 16 kD protein that is produced by adipocytes and induces weight loss in both normal and genetically obese ob/ob mice. ob/ob mice are obese, have multiple metabolic abnormalities, and exhibit impaired wound healing. Exogenous administration of leptin to these animals induces weight loss and corrects their metabolic defects. Leptin's effect on wound repair, however, has not been studied. Systemic administration of leptin at doses ranging from 0.1 to 10 mg/kg/day induced a highly significant acceleration in wound repair in ob/ob mice ( $p < 0.0001$ ), but not in db/db mice, indicating that leptin's effects on wound repair were mediated through the leptin receptor. We then investigated the possibility that leptin was acting directly at the wound site by administering leptin topically, and found that topical leptin also induced a dose dependent acceleration in wound repair ( $p < 0.0001$ ). In addition, we found that all forms of leptin receptor, including the signal transducing long form, were present in skin by RNase protection assay, and that leptin receptor localized to subcutaneous vessels of wounded skin by in situ hybridization. Finally, we investigated the possibility that leptin stimulated angiogenesis in wounds by analyzing wound hemoglobin and wound vessel density. Neither systemic nor topical leptin induced any significant changes in either parameter, suggesting that leptin accelerates wound repair by a mechanism other than stimulation of angiogenesis. In summary, both systemic and topical leptin accelerate wound repair in diabetic ob/ob mice, possibly via the direct interaction of leptin with its receptors in wounded skin, but do not appear to significantly stimulate wound angiogenesis. Further studies to better elucidate the mechanisms of leptin's effects on wound repair are warranted.